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Catalytic Hydrogenation of *N*-t-Butoxycarbonylindoles

Steven Coulton

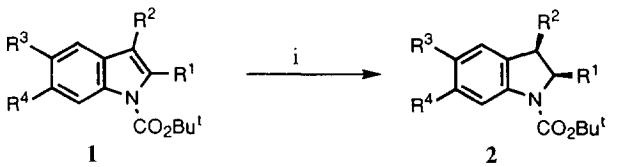
SmithKline Beecham Pharmaceuticals, Brockham Park, Betchworth, Surrey RH3 7AJ

Thomas L. Gilchrist* and Keith Graham

Chemistry Department, University of Liverpool, Liverpool L69 3BX, U.K.

Abstract: The rhodium catalysed hydrogenation of a range of *N*-t-butoxycarbonylindoles has been investigated. In most cases the hydrogenation proceeded smoothly at 200 psi in the presence of acetic acid to give the corresponding *N*-t-butoxycarbonyl-*cis*-2,3-dihydroindoles in high yield. Some indoles, in particular those bearing an acyl substituent at C-2 or at C-3, were not selectively reduced at the C-2–C-3 bond. Copyright © 1996 Elsevier Science Ltd

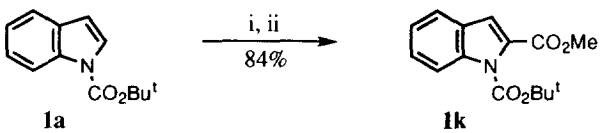
The reduction of indoles to indolines (2,3-dihydroindoles) can be achieved by catalytic hydrogenation and by a variety of other methods.[1] Catalytic hydrogenation usually requires forcing conditions and is sometimes not very selective. In the presence of a strong acid less forcing conditions are needed, probably because the indole is first protonated and it is the resulting iminium salt that is reduced. Several non catalytic methods of reduction, involving the use of sodium cyanoborohydride, trimethylamine–borane, *etc*., also take place in acidic media. As part of an investigation of routes to tricyclic β-lactams from indoles[2] we required a mild and selective method for the reduction of indole-2-acetic esters to the corresponding indolines. We found that the catalytic hydrogenation of the appropriate *N*-t-butoxycarbonylindoles over a rhodium catalyst provided such a method. We chose to use this method because Kaiser and Muchowski have shown that it is an efficient way of reducing *N*-t-butoxycarbonylpyrroles to the corresponding pyrrolidines.[3] Since the t-butoxycarbonyl (Boc) protecting group is readily introduced into indoles and easily removed from the products, we have carried out a more general investigation of the scope of the hydrogenation. In particular, we wanted to establish whether the reduction of 2,3-disubstituted indoles was stereoselective and what types of functional group could be tolerated. A series of *N*-t-butoxycarbonylindoles **1** was prepared and their catalytic reduction to the corresponding indolines **2** was investigated. We found that the reduction was best carried out at 200 psi over a rhodium–alumina catalyst in a 10:1 mixture of ethanol and acetic acid (Scheme 1).



1 **2**

Scheme 1 *Reagent:* i, H_2 (200 psi), Rh–Al_2O_3, EtOH–AcOH

The *N*-t-butoxycarbonylindoles that were prepared and the indolines that were successfully obtained from them are shown in the Table. *N*-t-Butoxycarbonylindole **1a** has previously been prepared by reaction of indole with t-butoxycarbonyl azide,[4] with t-butyl phenyl carbonate[5] and with di-t-butyl dicarbonate.[6] We found that the last method provided not only **1a** but other indoles **1b–1j** and **1l–1n** in high yield. Compound **1k** was prepared from **1a** by directed lithiation (Scheme 2). Except where indicated by references in the Table, these are new compounds. All the indolines isolated, with the exception of **2a** which has previously been prepared from indoline,[7] are also new compounds.



1a **1k**

Scheme 2 *Reagents*: i, BuLi, –78 °C; ii, $ClCO_2Me$

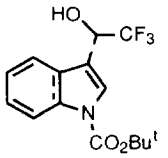
Table. *N*-t-Butoxycarbonylindoles **1** and *N*-t-Butoxycarbonylindolines **2** Prepared

1	R^1	R^2	R^3	R^4	**2** (%)
1a[6]	H	H	H	H	**2a**[7] (84)
1b[5]	Me	H	H	H	**2b** (86)
1c[5]	H	Me	H	H	**2c** (62)
1d[5]	Me	Me	H	H	**2d** (84)
1e	Me	Pr	H	H	**2e** (86)
1f[8]	Ph	H	H	H	**2f** (99)
1g[5]	$-(CH_2)_4-$		H	H	**2g** (79)
1h	$-CO(CH_2)_3-$		H	H	–
1i[9]	H	CHO	H	H	–
1j	H	$COCF_3$	H	H	–
1k[10]	CO_2Me	H	H	H	**2k**(99)
1l	CO_2Me	CO_2Me	H	H	**2l** (14)
1m	CO_2Me	Me	OMe	OMe	**2m** (84)
1n	Me	CO_2Et	$OCOBu^t$	H	**2n** (17)

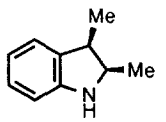
The hydrogenation proceeded smoothly in most cases to give a single product in high yield. The tetrahydrocarbazolone **1h** could not be hydrogenated, even when the reaction was continued for several days. The reduction of compounds **1l** and **1n** was very slow and when the reactions were discontinued after several days a large proportion of the starting material was recovered in each case. The yields of products shown in the Table do not take into account this recovered starting material. The 1,3-disubstituted indoles **1i** and **1j** both took up hydrogen but in neither case could the corresponding indoline be detected. The indole-3-carbaldehyde **1i** gave a complex mixture of products and no single component was identified. In the case of the 3-trifluoroacetylindole **1j** the product was identified as the alcohol **3** by comparison with a specimen

prepared by reduction of the ketone **1j** with sodium cyanoborohydride. The carbonyl group in **1j**, and possibly also in the aldehyde **1i**, is hydrogenated preferentially.

Only one isomer was formed in each of the hydrogenations of the 2,3-disubstituted indoles **1d**, **1e**, **1g**, **1l**, **1m** and **1n**. The product obtained from **1d** was shown to be the *cis* isomer **2d** by converting it to the known *cis*-2,3-dihydro-2,3-dimethylindole **4**. A comparison of the ^{1}H NMR spectrum of **4** with a published spectrum[11] confirmed its structure. This is the product to be expected if the catalytic hydrogenation takes place on the neutral indole. By analogy it is likely that all the other 2,3-disubstituted indoles also give exclusively the *cis* isomers as indicated in Scheme 1 but we have not established this unequivocally.



3



4

The 1-t-butoxycarbonyl substituent has thus been shown to promote the hydrogenation of the 2,3-double bond in indoles. The failure of the tetrahydrocarbazolone **1h** to undergo hydrogenation shows that a 2-acyl substituent inhibits the hydrogenation. These substituent effects are analogous to those found by Kaiser and Muchowski when they investigated the catalytic hydrogenation of pyrroles.[3]

EXPERIMENTAL

General ^{1}H NMR spectra were recorded on a Bruker ACE200 spectrometer operating at 200MHz and (where indicated) on a Bruker AMX400 instrument operating at 400 MHz. The solvent is deuteriochloroform except where indicated otherwise. Signals are singlets where no multiplicity is shown. Mass spectra were recorded under electron impact at 70 eV on a VG Micromass 7070E instrument. M.p.'s were recorded on a Reichert hot stage and are uncorrected. Flash column chromatography was performed with Merck 9385 silica as the stationary phase.

Methyl 5,6-dimethoxy-3-methylindole-2-carboxylate. To 5,6-dimethoxy-3-methylindole-2-carboxylic acid[12] (0.64 g, 2.7 mmol) was added an excess of ethereal diazomethane. After 3 h the reaction mixture was quenched by adding acetic acid. The solvent was removed *in vacuo* and the residue was subjected to column chromatography (ether) to give methyl 5,6-dimethoxy-3-methylindole-2-carboxylate (0.67, 99%), m.p. 163 °C (from ether) (Found: M, 249.100 $C_{13}H_{15}NO_4$ requires 249.100); $\nu_{max.}$ (nujol) 3342 and 1658 cm^{-1}; δ (200 MHz, $CDCl_3$) 2.56 (3 H, s, 3-Me), 3.91 (3 H, s), 3.92 (3 H, s), 3.95 (3 H, s), 6.79 (1 H, s), 6.97 (1 H, s) and 8.75 (1 H, bs, NH).

t-Butyl indole-1-carboxylate **1a**. This was prepared from indole and di-t-butyl dicarbonate according to a literature procedure.[6]

t-Butyl 2-methylindole-1-carboxylate **1b**.[5] To a stirred solution of 2-methylindole (2.80 g, 21.3 mmol) in dry dichloromethane (40 ml) was added 4-dimethylaminopyridine (2.87 g, 23.5 mmol) followed by di-*t*-butyl dicarbonate (6.52 g, 30 mmol). The solution was stirred at room temperature for 3 h. Evaporation of the solvent followed by column chromatography [dichloromethane–hexane (1:1)] gave the indole **1b** (4.19 g,

85%), m.p. 55 °C (from dichloromethane–hexane) (lit.,[5] 50–52 °C) (Found: C, 72.83; H, 7.43; N, 6.04. Calc for $C_{14}H_{17}NO_2$: C, 72.71; H, 7.41; N, 6.06%); $\nu_{max.}$ (nujol) 1735 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.67 (9 H, s, Bu^t), 2.59 (3 H, d, *J* 1.1 Hz, 2-Me), 6.31 (1 H, q, *J* 1.1 Hz, 3-H), 7.13–7.28 (2 H, m, 5-H and 6-H), 7.39–7.46 (1 H, m, 4-H) and 8.07–8.12 (1 H, m, 7-H); *m/z* 231 (M^+, 13%), 175 (42), 131 (56) and 57 (100).

The following indoles were prepared by the same method:

t-Butyl 3-methylindole-1-carboxylate **1c**[5] from 3-methylindole (0.78 g, 6.0 mmol). It was isolated (1.37 g, 100%) as an oil (Found: M, 231.1263. Calc. for $C_{14}H_{17}NO_2$: 231.1259); $\nu_{max.}$ (film) 1733 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.66 (9 H, s, Bu^t), 2.26 (3 H, d, *J* 1.1 Hz, 3-Me), 7.20–7.37 (3 H, m, 2-H, 5-H and 6-H), 7.50 (1 H, approx. dd, *J* 7.1 and 2.0 Hz, 4-H) and 8.11 (1 H, d, br, *J* 7.7 Hz, 7-H); *m/z* 231 (M^+, 15%), 175 (52), 130 (100) and 57 (92).

t-Butyl 2,3-dimethylindole-1-carboxylate **1d**[5] from 2,3-dimethylindole (0.417 g, 2.9 mmol). It was isolated (0.705 g, 100%) as a solid, m.p. 52 °C (from dichloromethane–hexane) (lit.,[5] 52 °C) (Found: C, 73.42; H, 7.84; N, 5.65. Calc for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71%); $\nu_{max.}$ (nujol) 1729 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.67 (9 H, s, Bu^t), 2.18 (3 H, s, 3-Me), 2.52 (3 H, s, 2-Me), 7.16–7.28 (2 H, m, 5-H and 6-H), 7.38–7.43 (1 H, m, 4-H) and 8.06–8.11 (1 H, m, 7-H); *m/z* 245 (M^+, 7%), 189 (36), 144 (61) and 57 (100).

t-Butyl 2-methyl-3-propylindole-1-carboxylate **1e** from 2-methyl-3-propylindole[13] (0.51 g, 2.9 mmol). It was isolated (0.80 g, 99%) as an oil (Found: C, 74.64; H, 8.53; N, 5.15. $C_{17}H_{23}NO_2$ requires: C, 74.69; H, 8.48; N, 5.12%); $\nu_{max.}$ (film) 1728 cm^{-1}; δ (200 MHz, $CDCl_3$) 0.95 (3 H, t, *J* 7.1 Hz, CH_2*Me*), 1.55–1.70 (2 H, m, CH_2CH_2Me) 1.68 (9 H, s, Bu^t), 2.52 (3 H, s, 2-Me), 2.63 (2 H, t, *J* 7.4 Hz, CH_2CH_2Me), 7.16–7.28 (2 H, m, 5-H and 6-H), 7.40–7.46(1 H, m, 4-H) and 8.05–8.14 (1 H, m, 7-H); *m/z* 273 (M^+, 16%), 217 (63), 144 (93) and 57 (100).

t-Butyl 2-phenylindole-1-carboxylate **1f** from 2-phenylindole (0.196 g, 1.0 mmol). It was isolated (0.297 g, 100%) as a solid, m.p. 65–66 °C (from dichloromethane–hexane) (Found: C, 77.85; H, 6.54; N, 4.74. $C_{19}H_{19}NO_2$ requires: C, 77.79; H, 6.53; N, 4.77%); $\nu_{max.}$ (nujol) 1735 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.30 (9 H, s, Bu^t), 6.55 (1 H, s, 3-H), 7.21–7.43 (7 H, m, Ph, C-5 and C-6), 7.55 (1 H, dd, *J* 7.2 and 1.1 Hz, 4-H) and 8.21 (1 H, approx. d, *J* 8.2 Hz, 7-H); *m/z* 293 (M^+, 5%), 237 (15), 193 (59) and 57 (100).

t-Butyl 1,2,3,4-tetrahydrocarbazole-9-carboxylate **1g**[5] from 1,2,3,4-tetrahydrocarbazole (0.33 g, 1.9 mmol). It was isolated (0.601 g, 100%) as an oil (Found: M, 271.1569. Calc. for $C_{17}H_{21}NO_2$: 271.1572); $\nu_{max.}$ (film) 1730 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.65 (9 H, s, Bu^t), 1.79–1.93 (4 H, m, 3-H and 4-H), 2.62–2.67 (2 H m, 4-H), 2.96–3.02 (2 H, m, 1-H), 7.15–7.27 (2 H, m, 6-H and 7-H), 7.36–7.40 (1 H, m, 5-H) and 8.09–8.14 (1 H, m, 8-H); *m/z* 271 (M^+, 8%), 215 (55), 143 (87) and 57 (100).

t-Butyl 1-oxo-1,2,3,4-tetrahydrocarbazole-9-carboxylate **1h** from 2,3,4,9-tetrahydrocarbazol-1-one[14] (0.53 g, 2.9 mmol). It was isolated (0.81 g, 99%) as a solid, m.p. 64–65 °C (from dichloromethane–hexane) (Found: C, 71.80; H, 6.74; N, 4.88. $C_{17}H_{19}NO_3$ requires C, 71.56; H, 6.71; N, 4.91%); $\nu_{max.}$ (nujol) 1718 and 1676 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.64 (9 H, s, Bu^t), 2.17–2.32 (2 H, m, 3-H),2.68 (2 H, t, *J* 7.1 Hz, 4-H), 2.98 (2 H, t, *J* 6.0 Hz, 2-H), 7.24–7.32 and 7.39–7.52 (each 1 H, m, 6-H and 7-H), 7.59–7.63 (1 H, m, 5-H) and 8.03–8.08 (1 H, m, 8-H); *m/z* 285 (M^+, 4%), 212 (11), 185 (100) and 57 (47).

t-Butyl 3-formylindole-1-carboxylate **1i**[9] from indole-3-carbaldehyde (0.60 g, 4.1 mmol). It was isolated (0.99 g, 98%) as a solid, m.p. 119–120 °C (from dichloromethane–hexane) (lit.,[9] m. p. 123–124 °C) (Found: C, 68.51; H, 6.13; N, 5.67. Calc. for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71%); $\nu_{max.}$ (nujol) 1729 and 1682 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.69 (9 H, s, Bu^t), 7.32–7.45 (2 H, m, 5-H and 6-H), 8.13–8.18 (1 H, m, 4-H), 8.23

(1 H, s, 2-H), 8.27–8.31(1 H, m, 7-H) and 10.11 (1 H, s, CHO); *m/z* 245 (M^+, 3%), 189 (12), 145 (20) and 57 (100).

t-Butyl 3-trifluoroacetylindole-1-carboxylate **1j** from 3-trifluoroacetylindole[15] (1.63 g, 7.65 mmol). It was isolated as a solid (2.20 g, 92%) m.p. 121 °C (from dichloromethane–hexane) (Found: C, 57.47; H, 4.50; N, 4.42. $C_{15}H_{14}F_3NO_3$ requires C, 57.51; H, 4.50; N, 4.47%); $\nu_{max.}$ (nujol) 1744 and 1689 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.73 (9 H, s, Bu^t), 7.36–7.52 (2 H, m, 5-H and 6-H), 8.13–8.22 (1 H, m, 4-H), 8.35–8.40(1 H, m, 7-H) and 8.45 (1 H, q, *J* 2.2 Hz, 2-H); *m/z* 313 (M^+, 7%), 213 (24), 144 (50) and 57(100).

t-Butyl (1) dimethyl (2,3) indole-1,2,3-tricarboxylate **1l** from dimethyl indole-2,3-dicarboxylate[16] (0.12 g, 0.51 mmol). It was isolated as a solid (0.17 g, 99%), m.p. 84 °C (from dichloromethane–hexane) (Found: C, 61.29; H, 5.77; N, 4.18. $C_{17}H_{19}NO_6$ requires C, 61.26; H, 5.75; N, 4.20%); $\nu_{max.}$ (nujol) 1744 and 1715 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.68 (9 H, s, Bu^t), 3.94 (3 H, s, OMe), 4.02 (3 H, s, OMe), 7.32–7.47 (2 H, m, 5-H and 6-H) and 8.13–8.18 (2 H, m, 4-H and 7-H); *m/z* 333 (M^+, 2%), 233 (31), 143 (32) and 57 (100).

t-Butyl (1) methyl (2) 5,6-dimethoxy-3-methylindole-1,2-dicarboxylate **1m** from methyl 5,6-dimethoxy-3-methylindole-2-carboxylate (0.40 g, 1.6 mmol). It was isolated as a solid (0.56 g, 100%), m.p. 69 °C (from dichloromethane–hexane) (Found: C, 61.88; H, 6.67; N, 3.95. $C_{18}H_{23}NO_6$ requires C, 61.88; H, 6.64; N, 4.01%); $\nu_{max.}$ (nujol) 1722 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.60 (9 H, s, Bu^t), 2.38 (3 H, s, 3-Me), 3.92 (3 H, s, OMe), 3.95 (3 H, s, OMe), 3.98 (3 H, s, OMe), 6.93 (1 H, s, 4-H) and 7.67 (1 H, s, 7-H); *m/z* 349 (M^+, 11%), 249 (99), 217 (100) and 57 (15).

t-Butyl (1) ethyl (3) 5-t-butoxycarboxy-2-methylindole-1,3-dicarboxylate **1n** from ethyl 5-hydroxy-2-methylindole-3-carboxylate[17] (0.63 g, 2.9 mmol). It was isolated as a solid (1.18 g, 98%) m.p. 81–82 °C (from ethanol) (Found: C, 62.99; H, 6.99; N, 3.31. $C_{22}H_{29}NO_7$ requires C, 62.99; H, 6.97; N, 3.34%); $\nu_{max.}$ (nujol) 1752, 1740 and 1691 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.45 (3 H, t, *J* 7.1 Hz), 1.56 (9 H, s, Bu^t-5), 1.69 (9 H, s, Bu^t-1), 2.98 (3 H, s, 2-Me), 4.41 (2 H, q, *J* 7.1 Hz), 7.09 (1 H, dd, *J* 9.3 and 2.2 Hz, 6-H), 7.88 (1 H, d, *J* 2.2 Hz, 4-H) and 8.06 (1 H, d, *J* 9.3 Hz, 7-H); *m/z* 419 (M^+, 2%), 319 (5), 224 (36) and 57 (100).

t-Butyl (1) methyl (2) indole-1,2-dicarboxylate **1k**. To an oven-dried flask was added dry THF (50 ml) followed by t-butyllithium (12.3 ml, 1.7 M in pentane, 20.9 mmol) and the solution was cooled to – 78 °C. t-Butyl indole-1-carboxylate **1a** (2.45 g, 11.3 mmol) in dry THF (20 ml) was added slowly. The resulting solution was stirred at – 78 °C for 1 h. After 1 h methyl chloroformate (2.47 g, 25.9 mmol) was added and the reaction mixture was allowed to warm to room temperature. It was then quenched by the careful addition of water (20 ml). The organic components were extracted with ethyl acetate (3 x 40 ml), the solution was dried over $MgSO_4$ and the solvent was removed *in vacuo*. The crude residue was subjected to column chromatography [dichloromethane: hexane (1:1)] to give *the indole* **1k** (2.60 g, 84 %) as an oil (Found: M, 275.1155. Calc. for $C_{15}H_{17}NO_4$: 275.1157); $\nu_{max.}$ (film) 1739 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.62 (9 H, s, Bu^t), 3.92 (3 H, s, OMe), 7.10 (1 H, s, 3-H), 7.22–7.30 and 7.37–7.46 (each 1 H, m, 5-H and 6-H), 7.58–7.62 (1 H, m, 4-H) and 8.07–8.12 (1 H, m, 7-H); *m/z* 275 (M^+, 6%), 175 (83%), 143 (100) and 57 (94).

t-Butyl 2,3-dihydroindole-1-carboxylate **2a**.[7] To a 25 cm^3 hydrogenation vessel was added a solution of t-butyl indole-1-carboxylate **1a** (0.26 g, 1.2 mmol) in ethanol (4.5 ml) and glacial acetic acid (0.5 ml) followed by 5% rhodium on alumina (30 mg). The hydrogenation vessel was flushed with hydrogen three times and sealed at a pressure of 200 psi. The reaction mixture was vigorously stirred and the progress of the reaction was followed by the uptake of hydrogen and by TLC. When the starting material was no longer present the solvents were removed *in vacuo* and the crude residue was subjected to column chromatography [dichloromethane–hexane (1:1)]. This gave the dihydroindole **2a** (0.22 g, 84%) as an oil (Found: M, 219.126.

Calc. for $C_{13}H_{17}NO_2$: 219.126; $\nu_{max.}$ (film) 1700 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.57 (9 H, s, Bu^t), 3.08 (2 H, t, *J* 8.8 Hz, 3-CH_2), 3.97 (2 H, t, *J* 8.8 Hz, 2-CH_2), 6.88–6.96 (1 H, m), 7.11–7.19 (2 H, m) and 7.81 (1 H, br, 7-H); *m/z* 219 (M^+, 7%), 163 (60), 118 (59) and 57 (100).

The following dihydroindoles were prepared by the same method:

t-Butyl 2,3-dihydro-2-methylindole-1-carboxylate **2b** from the indole **1b** (0.23 g, 1.0 mmol). Column chromatography gave **2b** (0.20 g, 86%) as an oil which slowly crystallised, m.p. 30 °C (Found: C, 72.41; H, 8.40; N, 6.10. $C_{14}H_{19}NO_2$ requires C, 72.07; H, 8.21; N, 6.00%); $\nu_{max.}$ (nujol) 1700 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.28 (3 H, d, *J* 6.6 Hz, 2-Me), 1.57 (9 H, s, Bu^t), 2.59 (1 H, dd, *J* 15.9 and 2.2 Hz, 3-H), 3.33 (1 H, dd, *J* 15.9 and 9.9 Hz, 3-H), 4.41–4.61 (1 H, m, 2-H), 6.89–6.97 (1 H, m,), 7.12–7.20 (2 H, m) and 7.69 (1 H, br, 7-H); *m/z* 233 (M^+, 16%), 177 (99), 118 (100) and 57 (100).

t-Butyl 2,3-dihydro-3-methylindole-1-carboxylate **2c** from the indole **1c** (0.16 g, 0.69 mmol). Column chromatography gave **2c** (0.10 g, 62%) as an oil (Found: C, 72.20; H, 8.25; N, 6.01. $C_{14}H_{19}NO_2$ requires C, 72.07; H, 8.21; N, 6.00%); $\nu_{max.}$ (film) 1705 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.33 (3 H, d, *J* 6.6 Hz, 3-Me), 1.58 (9 H, s, Bu^t), 3.34–3.55 (2 H, m, 2-H and 3-H), 4.10–4.20 (1 H, dd, *J* 10.4 and 9.3 Hz, 2-H), 6.92–6.99 (1 H, m), 7.12–7.21 (2 H, m) and 7.81 (1 H, br, 7-H); *m/z* 233 (M^+, 10%), 177 (73), 118 (78) and 57 (100).

t-Butyl cis-*2,3-dihydro-2,3-dimethylindole-1-carboxylate* **2d** from the indole **1d** (0.26 g, 1.1 mmol). Column chromatography gave **2d** (0.22 g, 84%) as an oil (Found: C, 72.62; H, 8.53; N, 5.70. $C_{15}H_{21}NO_2$ requires C, 72.84; H, 8.56; N, 5.66%); $\nu_{max.}$ (film) 1695 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.12 (3 H, d, *J* 6.6 Hz, 2-Me) 1.29 (3 H, d, *J* 7.1 Hz, 3-Me), 1.57 (9 H, s, Bu^t), 3.51 (1 H, dq, *J* 8.0 and 7.1 Hz, 3-H), 4.52 (1 H, dq, *J* 8.0 and 6.6 Hz, 2-H), 6.93–7.00 (1 H, m), 7.08–7.21 (2 H, m) and 7.65 (1 H, br, 7-H),; *m/z* 247 (M^+, 10%), 177 (75), 147 (9) 132 (88) and 57 (100).

t-Butyl cis-*2,3-dihydro-2-methyl-3-propylindole-1-carboxylate* **2e** from the indole **1e** (0.22 g, 0.80 mmol). Column chromatography gave **2e** (0.19 g, 86%) as an oil (Found: C, 73.95; H, 9.20; N, 5.03. $C_{17}H_{25}NO_2$ requires : C, 74.14; H, 9.15; N, 5.09%); $\nu_{max.}$ (film) 1707 cm^{-1}; δ (200 MHz, $CDCl_3$) 0.99 (3 H, t, *J* 6.6 Hz, CH_2Me) 1.08 (3 H, d, *J* 6.6 Hz, 2-Me), 1.41–1.67 (4 H, m), 1.57 (9 H, s, Bu^t), 3.30–3.41 (2 H, m, 2-H and 3-H), 4.46–4.61 (1 H, m, 2-H), 6.92–6.99 (1 H, m), 7.11–7.20 (2 H, m) and 7.64 (1 H, br, 7-H), ; *m/z* 275 (M^+, 2%), 219 (12), 176 (16) and 57 (100).

t-Butyl 2,3-dihydro-2-phenylindole-1-carboxylate **2f** from the indole **1f** (0.17 g, 0.72 mmol). Column chromatography gave **2f** (0.17 g, 99%), m. p. 111 °C ((from dichloromethane–hexane) (Found: C, 76.99; H, 7.26; N, 4.62. $C_{19}H_{21}NO_2$ requires C, 77.26; H, 7.17; N, 4.74%); $\nu_{max.}$ (nujol) 1697 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.58 (9 H, s, Bu^t), 2.95 (1 H, dd, *J* 16.4 and 3.6 Hz, 3-H), 3.67 (1 H, dd, *J* 16.4 and 11.0 Hz, 3-H), 5.33–5.40 (1 H, m, 2-H), 6.93–6.97 (1 H, m), 7.11–7.33 (8 H, m) and 7.90 (1 H, br, 7-H); *m/z* 295 (M^+, 10%), 239 (97), 194 (82) 118 (85) and 57 (100).

t-Butyl cis-*1,2,3,4,4a,9a-hexahydrocarbazole-9-carboxylate* **2g** from the tetrahydrocarbazole **1g** (0.20 g, 0.74 mmol). Column chromatography gave **2g** (0.16 g, 79%) as an oil (Found: C, 74.73; H, 8.53; N, 5.17. $C_{17}H_{23}NO_2$ requires C, 74.69; H, 8.48; N, 5.12%); $\nu_{max.}$ (film) 1701 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.09–1.33 (4 H, m) 1.57–1.68 (2 H, m), 1.58 (9 H, s, Bu^t), 2.01–2.29 (2 H, m), 3.38–3.49 (1 H, m, 4a-H), 4.29–4.42 (1 H, m, 9a-H), 6.93–7.01 (1 H, m), 7.11–7.21 (2 H, m) and 7.68 (1 H, br, 8-H), ; *m/z* 273 (M^+, 9%), 217 (100), 130 (67%) and 57 (100).

t-Butyl (1) methyl (2) 2,3-dihydroindole-1,2-dicarboxylate **2k** from the indole **1k** (0.17 g, 0.62 mmol). Column chromatography gave **2k** (0.17 g, 99%), m.p. 40–42 °C (from dichloromethane–hexane) (Found: C,

65.00; H, 6.95; N, 5.00. $C_{15}H_{19}NO_4$ requires C, 64.97; H, 6.91; N, 5.05%); $\nu_{max.}$ (film) 1755 and 1712 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.51 (9 H, s, Bu^t), 3.09 (1 H, dd, *J* 16.5 and 4.9 Hz, 3-H), 3.48 (1 H, dd, *J* 16.5 and 11.6 Hz, 3-H), 3.74 (3 H, s, 2-OMe), 4.79 (1 H, br m, 2-H), 6.89–6.97 (1 H, m), 7.08–7.22 (2 H, m), 7.51 (1 H, br, 7-H), ; *m/z* 277 (M^+, 5%), 177 (17), 118 (100) and 57 (44).

t-Butyl (1) dimethyl (2,3) 2,3-dihydroindole-1,2,3-tricarboxylate **2l** from the indole **1l** (0.14 g, 0.42 mmol). Hydrogenation was very slow. Column chromatography [dichloromethane–hexane (1:1)] gave **2l** (0.02 g, 14%) as an oil (Found: C, 60.46; H, 6.43; N, 3.86; M, 335.137. $C_{17}H_{21}NO_6$ requires C, 60.89; H, 6.31; N, 4.18%; M, 335.137); $\nu_{max.}$ (film) 1745 and 1719 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.51 (9 H, s, Bu^t), 3.73 (3 H, s, OMe), 3.77 (3 H, s, OMe), 4.64 (1 H, d, *J* 11.0 Hz, 3-H), 5.10 (1 H, d, *J* 11.0 Hz, 2-H), 6.96–7.03 (1 H, m), 7.17–7.31 (2 H, m) and 7.90 (1 H, br, 7-H); *m/z* 335 (M^+, 5%), 235 (35), 176 (100) and 57(89). The majority of the triester **1l** (0.12 g, 86%) was recovered.

t-Butyl (1) methyl (2) 2,3-dihydro-5,6-dimethoxy-3-methylindole-1,2-carboxylate **2m** from the indole **1m** (0.19 g, 0.57 mmol). Column chromatography gave **2m** (0.16g, 84%), m.p. 74 °C (from dichloromethane–hexane) (Found: C, 61.53; H, 7.22; N, 3.94. $C_{18}H_{25}NO_6$ requires C, 61.53; H, 7.17; N, 3.99%); $\nu_{max.}$ (film) 1743 and 1692 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.26 (3 H, d, *J* 7.2 Hz, 3-Me), 1.49 (9 H, s, Bu^t), 3.74 (3 H, s, OMe), 3.84 (3 H, s, OMe), 3.92 (3 H, s, OMe), 3.80–4.00 (1 H, m, 3-H), 4.88 (1 H, d, *J* 11.0 Hz, 2-H), 6.64 (1 H, s, 4-H) and 7.63 (1 H, s, 7-H); *m/z* 351 (M^+, 20%), 251 (77), 192 (100) and 57 (55).

t-Butyl (1) ethyl (3) 5-t-butoxycarboxy-2,3-dihydro-2-methylindole-1,3-dicarboxylate **2n** from the indole **1n** (0.42 g, 1.0 mmol). Hydrogenation was slow. Column chromatography gave **2n** (0.07 g, 17%) as an oil (Found: M, 421.210. $C_{22}H_{31}NO_7$ requires M, 421.210); δ (200 MHz, $CDCl_3$) 1.20 (3 H, d, *J* 6.6 Hz, 2-Me), 1.33 (3 H, t, *J* 7.1 Hz, $CH_2\underline{Me}$), 1.55 (9 H, Bu^t), 1.56 (9 H, Bu^t), 4.27 (2 H, q, *J* 7.1 Hz, $C\underline{H}_2Me$), 4.41 (1 H, d, *J* 9.3 Hz, 3-H), 4.70–4.90 (1 H, m, 2-H), 6.98–7.04 (1 H, m, 6-H), 7.17–7.19 (1 H, m, 4-H) and 7.73 (1 H, br, 7-H); m/z 421 (M+, 1%), 321 (3),221 (32) and 57 (100). The indole **1n** (76%) was recovered.

t-Butyl 3-*(1,1,1-trifluoro-2-hydroxyethyl) indole-1-carboxylate* **3.** To a stirred suspension of t-butyl-3-trifluoroacetylindole-1-carboxylate (0.28 g, 0.90 mmol) in methanol (10 ml) was added sodium cyanoborohydride (0.45 g, 7.17 mmol). The resulting solution was stirred at room temperature overnight. The reaction mixture was quenched by the addition of water and the product was extracted with ethyl acetate (3 x 30 ml). The extracts were combined, dried over $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography (dichloromethane) gave the indole **3** (0.27 g, 96%), m.p. 100–102 °C (from hexane) (Found: C, 57.12; H, 5.10; N, 4.45; M^+, 315.108. $C_{15}H_{16}F_3NO_3$ requires C, 57.14; H, 5.12; N, 4.44%; M^+, 315.108); ν_{max} (film) 3441, 2928 and 1744 cm^{-1}: δ (200 MHz, $CDCl_3$) 1.68 (9 H, s, Bu^t), 2.57 (1 H, d, *J* 5.5 Hz, OH), 5.55–5.41 (1 H, m, $C\underline{H}$(OH)), 7.26–7.41 (2 H, m, Ar-H), 7.67–7.71 (1 H, m, Ar-H), 7.76 (1 H, s, 2-H) and 8.16–8.20 (1 H, m, Ar-H); m/z 315 (M^+, 3%), 259 (17), 146 (32) and 57 (100).

The alcohol **3** was identified (TLC, NMR, MS) as the major component of the mixture resulting from the hydrogenation of the indole **1j** under the general conditions described above.

cis-*2,3-Dihydro-2,3-dimethylindole* **4**.[11] Trifluoroacetic acid (1 ml) was added to a solution of the dihydroindole **2d** (0.21 g, 0.8 mmol) in dichloromethane (10 ml). The solution was stirred overnight at room temperature and poured into saturated aq. sodium hydrogencarbonate. The organic product was extracted with dichloromethane, the solution dried over MgSO4 and concentrated *in vacuo*. The residue was subjected to column chromatography (dichloromethane) to give 2,3-dimethylindole (0.12 g, 96%) as an oil (Found: M, 247.157. Calc. for $C_{15}H_{21}NO_2$: 247.157); $\nu_{max.}$ (film) 3369 and 1609 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.12 (3 H, d, *J* 6.6 Hz, 2-Me) 1.17 (3 H, d, *J* 7.1 Hz, 3-Me), 3.19 (1 H, br, NH), 3.26 (1 H, dq, *J* 7.9 and 7.1 Hz, 3-H),

3.93 (1 H, dq, *J* 7.9 and 6.6 Hz, 2-H), 6.61 (1 H, d, *J* 7.7 Hz, Ar-H), 6,73 (1 H, ddd, *J* 7.7, 7.1 and 1.1 Hz, Ar-H) and 6.98–7.08 (2 H, m, Ar-H); *m/z* 247 (M^+, 10%), 177 (75), 147 (9) 132 (88) and 57(100).

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